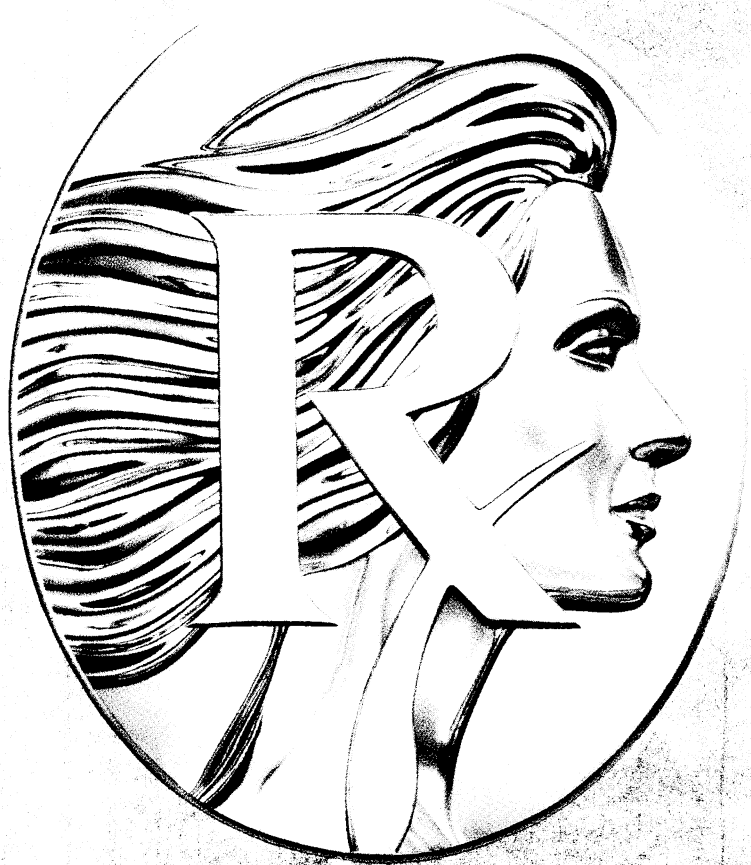


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†Constipation, which is easily managed in most patients, is the most commonly reported side effect of Calan SR.

*Verapamil should be administered cautiously to patients with impaired renal function.

BRIEF SUMMARY

Contraindications: Severe LV dysfunction (see *Warnings*), hypotension (systolic pressure < 90 mm Hg) or cardiogenic shock, sick sinus syndrome (if no pacemaker is present), 2nd- or 3rd-degree AV block (if no pacemaker is present), atrial flutter/fibrillation with an accessory bypass tract (eg, WPW or LGL syndromes), hypersensitivity to verapamil.

Warnings: Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction < 30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta-blocker. Control milder heart failure with optimum digitalization and/or diuretics before Calan SR is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported. Several cases have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving I.V. verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (2nd- and 3rd-degree, 0.8%). Development of marked 1st-degree block or progression to 2nd- or 3rd-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, 2nd-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

Precautions: Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdosage. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol and propranolol clearance may occur when either drug is administered concomitantly with verapamil. A variable effect has been seen with combined use of atenolol. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digoxin. The digoxin dose should be reduced when verapamil is given, and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents.

References: 1. Data on file, Searle. 2. Edmonds D, Würth JP, Baumgart P, et al. Twenty-four-hour monitoring of blood pressure during calcium antagonist therapy. In: Fleckenstein A, Laragh SH, eds. *Hypertension—the Next Decade: Verapamil In Focus*. New York, NY: Churchill Livingstone; 1987:94-100. 3. Midtbø KA. Effects of long-term verapamil therapy on serum lipids and other metabolic parameters. *Am J Cardiol*. 1990;66:131-151. 4. Fagher B, Henningsen N, Hultén L, et al. Antihypertensive and renal effects of enalapril and slow-release verapamil in essential hypertension. *Eur J Clin Pharmacol*. 1990;39(suppl 1):S41-S43. 5. Schmeider RE, Messerli FH, Garavaglia GE, et al. Cardiovascular effects of verapamil in patients with essential hypertension. *Circulation*. 1987;75:1030-1036. 6. Midtbø K, Lauve O, Hals O. No metabolic side effects of long-term treatment with verapamil in hypertension. *Angiology*. 1988;39:1025-1029.

Disopyramide should not be given within 48 hours before or 24 hours after verapamil administration. Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Concomitant use of lithium and verapamil may result in an increased sensitivity to lithium (neurotoxicity), with either no change or an increase in serum lithium levels; however, it may also result in a lowering of serum lithium levels. Patients receiving both drugs must be monitored carefully. Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporin. Verapamil may inhibit the clearance and increase the plasma levels of theophylline. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing); dosage reduction may be required. There was no evidence of a carcinogenic potential of verapamil administered to rats for 2 years. A study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use.

Adverse Reactions: Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF, pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia: HR < 50/min (1.4%), AV block: total 1°, 2°, 3° (1.2%), 2° and 3° (0.8%), rash (1.2%), flushing (0.6%), elevated liver enzymes, reversible non-obstructive paralytic ileus. The following reactions, reported in 1.0% or less of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope, diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia, ecchymosis or bruising, cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, skininess, somnolence, arthralgia and rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme, blurred vision, gynecomasia, galactorrhea/hyperprolactinemia, increased urination, spotty menstruation, impotence.

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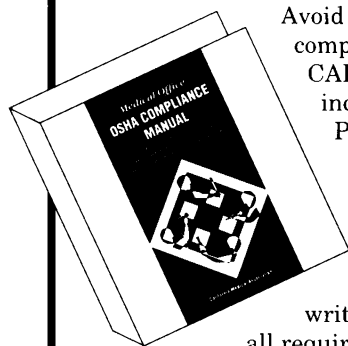
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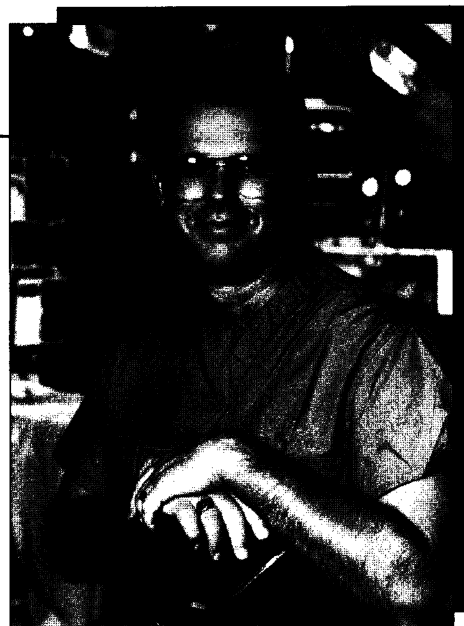
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PAGE PROFILE



Vaughn A. Starnes, M.D. has joined the University of Southern California School of Medicine.

Vaughn A. Starnes, M.D., has joined the University of Southern California School of Medicine as Professor of Surgery, Chief of the Division of Cardiothoracic Surgery and Director of the USC Cardiothoracic Center at USC University Hospital, Childrens Hospital Los Angeles and Los Angeles County+USC Medical Center. Dr. Starnes is a world-recognized leader and innovator in adult and pediatric heart, heart-lung and lung transplantation and treatment of congenital heart disease.

In 1984 Dr. Starnes was accepted to the Stanford Cardiothoracic program, where he completed two years as a resident in cardiovascular surgery, and one year as chief resident in cardiac transplantation under the guidance of Norman Shumway, M.D.

In 1988 Dr. Starnes was appointed director of Stanford's heart-lung transplantation program, and later became chief of pediatric heart surgery and director of the transplant program at Stanford's Lucile Salter Packard Childrens Hospital. He performed about 400 adult and pediatric cardiac cases annually at Stanford. In addition to his adult cardiothoracic surgical expertise, Dr. Starnes earned a national reputation for his work in pediatrics.

Dr. Starnes also pioneered lung and heart-lung transplant procedures in children that previously had only been performed on adults. In 1991 he was the first surgeon to transplant the left upper lobe of a 2-year-old donor into a newborn with pulmonary hypertension who could not be weaned off ECMO (Extracorporeal Membrane Oxygenation). In 1992, he performed the first lung transplant on a baby with congenital diaphragmatic hernia.

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The USC Cardiothoracic Center is one of a handful of centers in the country to provide a comprehensive range of adult and pediatric cardiovascular services including adult and pediatric heart, heart-lung and lung transplantation.

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The Center also specializes in the treatment of infants with congenital heart defects including hypoplastic left heart syndrome, aortic valve disease, and transposition of the great vessels.

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At the Center, cardiologists, cardiothoracic surgeons, vascular surgeons, radiologists, interventional radiologists and allied medical professionals pool their extensive knowledge and expertise to provide patients with the full range of diagnostic and treatment alternatives.

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As a university-based program, the Center is actively engaged in research. Specialists identify clinical problems and then seek the answer in the laboratory. Patients benefit from this link between bench and bedside, which promises to provide a better understanding of the physiology of the disease process.

Community Resource

As a vital component of the USC School of Medicine, the USC Cardiothoracic Center serves as a key educational resource for community-based and referring physicians. Physicians are encouraged to contact the Center through PACE to obtain telephone consultations, and access information regarding new patient care techniques, medications and research protocols to receive assistance with patient management concerns.

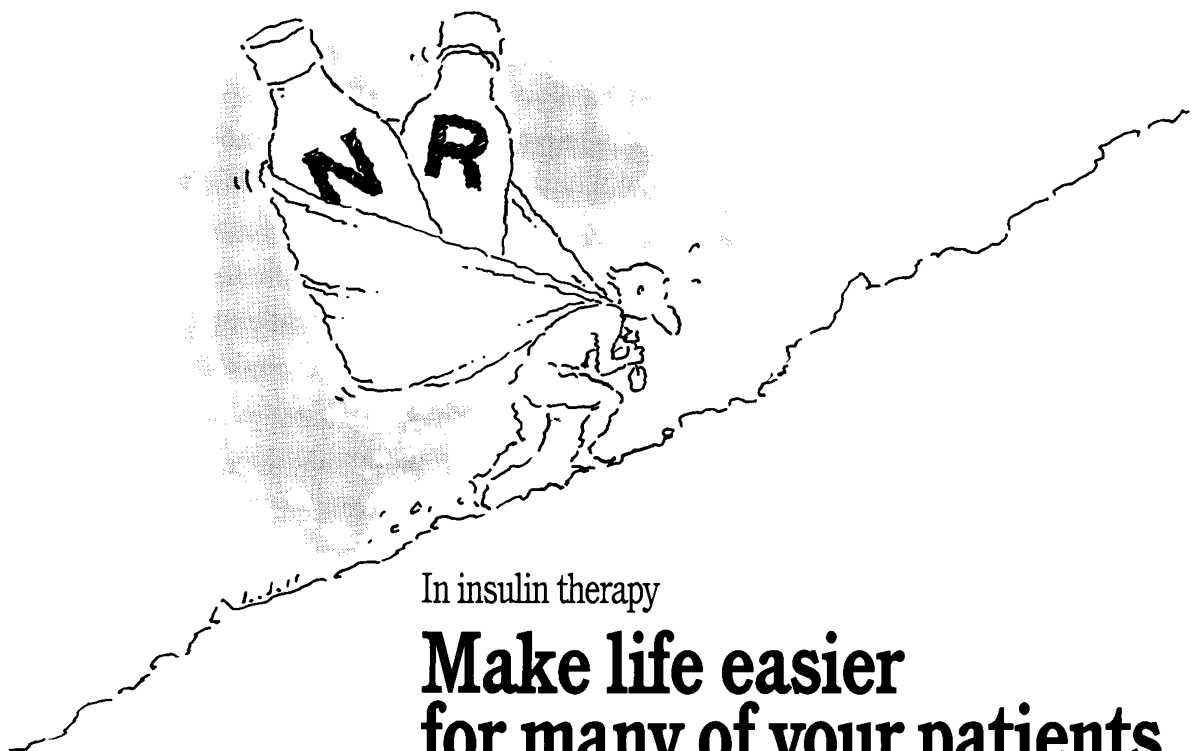
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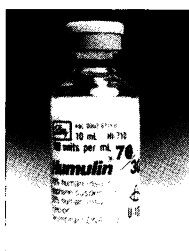




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BRIEF SUMMARY

CARDIZEM® CD (diltiazem hydrochloride) Capsules
CARDIZEM® SR (diltiazem hydrochloride) Sustained Release Capsules

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, (3) patients with hypotension (less than 90 mm Hg systolic), (4) patients who have demonstrated hypersensitivity to the drug, and (5) patients with acute myocardial infarction and pulmonary congestion documented by X-ray on admission.

WARNINGS

1. Cardiac Conduction. CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (13 of 3,007 patients or 0.43%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.

2. Congestive Heart Failure. Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). An acute study of oral diltiazem in patients with impaired ventricular function (ejection fraction 9.4% ± 6%) showed improvement in indices of ventricular function without significant decrease in contractile function (dp/dt). Worsening of congestive heart failure has been reported in patients with preexisting impairment of ventricular function. Experience with the use of CARDIZEM in combination with beta-blockers in patients with impaired ventricular function is limited. Caution should be exercised when using this combination.

3. Hypotension. Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.

4. Acute Hepatic Injury. Mild elevations of transaminases with and without concomitant elevation in alkaline phosphatase and bilirubin have been observed in clinical studies. Such elevations were usually transient and frequently resolved even with continued diltiazem treatment. In rare instances, significant elevations in enzymes such as alkaline phosphatase, LDH, SGOT, SGPT, and other phenomena consistent with acute hepatic injury have been noted. These reactions tended to occur early after therapy initiation (1 to 8 weeks) and have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in some cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS

General. CARDIZEM is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Dermatological events (see ADVERSE REACTIONS section) may be transient and may disappear despite continued use of CARDIZEM. However, skin eruptions progressing to erythema multiforme and/or exfoliative dermatitis have also been infrequently reported. Should a dermatologic reaction persist, the drug should be discontinued.

Drug Interaction. Due to the potential for additive effects, caution and careful titration are warranted in patients receiving CARDIZEM concomitantly with any agents known to affect cardiac contractility and/or conduction. (See WARNINGS.) Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

As with all drugs, care should be exercised when treating patients with multiple medications. CARDIZEM undergoes biotransformation by cytochrome P-450 mixed function oxidase. Coadministration of CARDIZEM with other agents which follow the same route of biotransformation may result in the competitive inhibition of metabolism. Dosages of similarly metabolized drugs such as cyclosporin, particularly those of low therapeutic ratio or in patients with renal and/or hepatic impairment, may require adjustment when starting

or stopping concomitantly administered CARDIZEM to maintain optimum therapeutic blood levels.

Beta-blockers: Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers is usually well tolerated, but available data are not sufficient to predict the effects of concomitant treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities.

Administration of CARDIZEM (diltiazem hydrochloride) concomitantly with propranolol in five normal volunteers resulted in increased propranolol levels in all subjects and bioavailability of propranolol was increased approximately 50%. If combination therapy is initiated or withdrawn in conjunction with propranolol, an adjustment in the propranolol dose may be warranted. (See WARNINGS.)

Cimetidine: A study in six healthy volunteers has shown a significant increase in peak diltiazem plasma levels (58%) and area-under-the-curve (53%) after a 1-week course of cimetidine at 1,200 mg per day and diltiazem 60 mg per day. Ranitidine produced smaller, nonsignificant increases. The effect may be mediated by cimetidine's known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of diltiazem. Patients currently receiving diltiazem therapy should be carefully monitored for a change in pharmacological effect when initiating and discontinuing therapy with cimetidine. An adjustment in the diltiazem dose may be warranted.

Digitalis: Administration of CARDIZEM with digoxin in 24 healthy male subjects increased plasma digoxin concentrations approximately 80%. Another investigator found no increase in digoxin levels in 12 patients with coronary artery disease. Since there have been conflicting results regarding the effect of digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing CARDIZEM therapy to avoid possible over- or under-digitalization. (See WARNINGS.)

Anesthetics: The depression of cardiac contractility, conductivity, and automaticity as well as the vascular dilation associated with anesthetics may be potentiated by calcium channel blockers. When used concomitantly, anesthetics and calcium blockers should be titrated carefully.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats at oral dosage levels of up to 100 mg/kg/day, and a 21-month study in mice at oral dosage levels of up to 30 mg/kg/day showed no evidence of carcinogenicity. There was also no mutagenic response in vitro or in vivo in mammalian cell assays or in vitro in bacteria. No evidence of impaired fertility was observed in a study performed in male and female rats at oral dosages of up to 100 mg/kg/day.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded from these studies.

The adverse events described below represent events observed in clinical studies of hypertensive patients receiving either CARDIZEM Tablets or CARDIZEM SR Capsules as well as experiences observed in studies of angina and during marketing. The most common events in hypertension studies are shown in a table with rates in placebo patients shown for comparison. Less common events are listed by body system; these include any adverse reactions seen in angina studies that were not observed in hypertension studies. In all hypertensive patients taking CARDIZEM Tablets or CARDIZEM SR Capsules studied (over 900), the most common adverse events were edema (9%), headache (8%), dizziness (6%), asthenia (5%), sinus bradycardia (3%), flushing (3%), and first-degree AV block (3%). Only edema and perhaps bradycardia and dizziness were dose related.

DOUBLE BLIND PLACEBO CONTROLLED HYPERTENSION TRIALS

ADVERSE	CARDIZEM N=315 # PTS (%)	PLACEBO N=311 # PTS (%)
Headache	38 (12%)	17 (8%)
AV Block First Degree	24 (7.6%)	4 (1.9%)
Dizziness	22 (7%)	6 (2.8%)
Edema	19 (6%)	2 (0.9%)
Bradycardia	19 (6%)	3 (1.4%)
ECG Abnormality	13 (4.1%)	3 (1.4%)
Asthenia	10 (3.2%)	1 (0.5%)
Constipation	5 (1.6%)	2 (0.9%)
Dyspepsia	4 (1.3%)	1 (0.5%)
Nausea	4 (1.3%)	2 (0.9%)
Palpitations	4 (1.3%)	2 (0.9%)
Polyuria	4 (1.3%)	2 (0.9%)
Somnolence	4 (1.3%)	—
Alk Phos Increase	3 (1%)	1 (0.5%)
Hypotension	3 (1%)	1 (0.5%)
Insomnia	3 (1%)	1 (0.5%)
Rash	3 (1%)	1 (0.5%)
AV Block Second Degree	2 (0.6%)	—

The following table presents the most common adverse reactions reported in placebo-controlled trials in patients receiving CARDIZEM CD up to 360 mg with rates in placebo patients shown for comparison.

ADVERSE REACTION	CARDIZEM CD N=394	PLACEBO N=175
HEADACHE	9.0%	8.0%
BRADYCARDIA	4.3%	2.3%
EDEMA	3.7%	2.3%
DIZZINESS	3.1%	3.4%
ECG ABNORMALITY	3.1%	2.9%
AV BLOCK FIRST DEGREE	2.9%	—
ASTHENIA	1.9%	1.7%

In clinical trials of CARDIZEM CD Capsules, CARDIZEM Tablets, and CARDIZEM SR Capsules involving over 3000 patients, the most common events (ie, greater than 1%) were edema (4.9%), headache (4.9%), dizziness (3.5%), asthenia (2.7%), first-degree AV block (2.2%), bradycardia (1.6%), flushing (1.5%), nausea (1.4%), rash (1.3%), and dyspepsia (1.2%).

In addition, the following events were reported infrequently (less than 1%).

Cardiovascular: Angina, arrhythmia, AV block (second- or third-degree), bundle branch block, congestive heart failure, ECG abnormalities, hypotension, palpitations, syncope, tachycardia, ventricular extrasystoles.

Nervous System: Abnormal dreams, amnesia, depression, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.

Gastrointestinal: Anorexia, constipation, diarrhea, dry mouth, dysgeusia, mild elevations of SGOT, SGPT, LDH, and alkaline phosphatase (see hepatic warnings), thirst, vomiting, weight increase.

Dermatological: Patches, photosensitivity, pruritus, urticaria.

Other: Amblyopia, CPK increase, dyspnea, epistaxis, eye irritation, hyperglycemia, hyperuricemia, impotence, muscle cramps, nasal congestion, nocturia, osteoarthralgia, polyuria, sexual difficulties.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, erythema multiforme, exfoliative dermatitis, extrapyramidal symptoms, gingival hyperplasia, hemolytic anemia, increased bleeding time, leukopenia, purpura, retinopathy, and thrombocytopenia. In addition, events such as myocardial infarction have been observed which are not readily distinguishable from the natural history of the disease in these patients. A number of well-documented cases of generalized rash, characterized as leukocytoclastic vasculitis, have been reported. However, a definitive cause and effect relationship between these events and CARDIZEM therapy is yet to be established.

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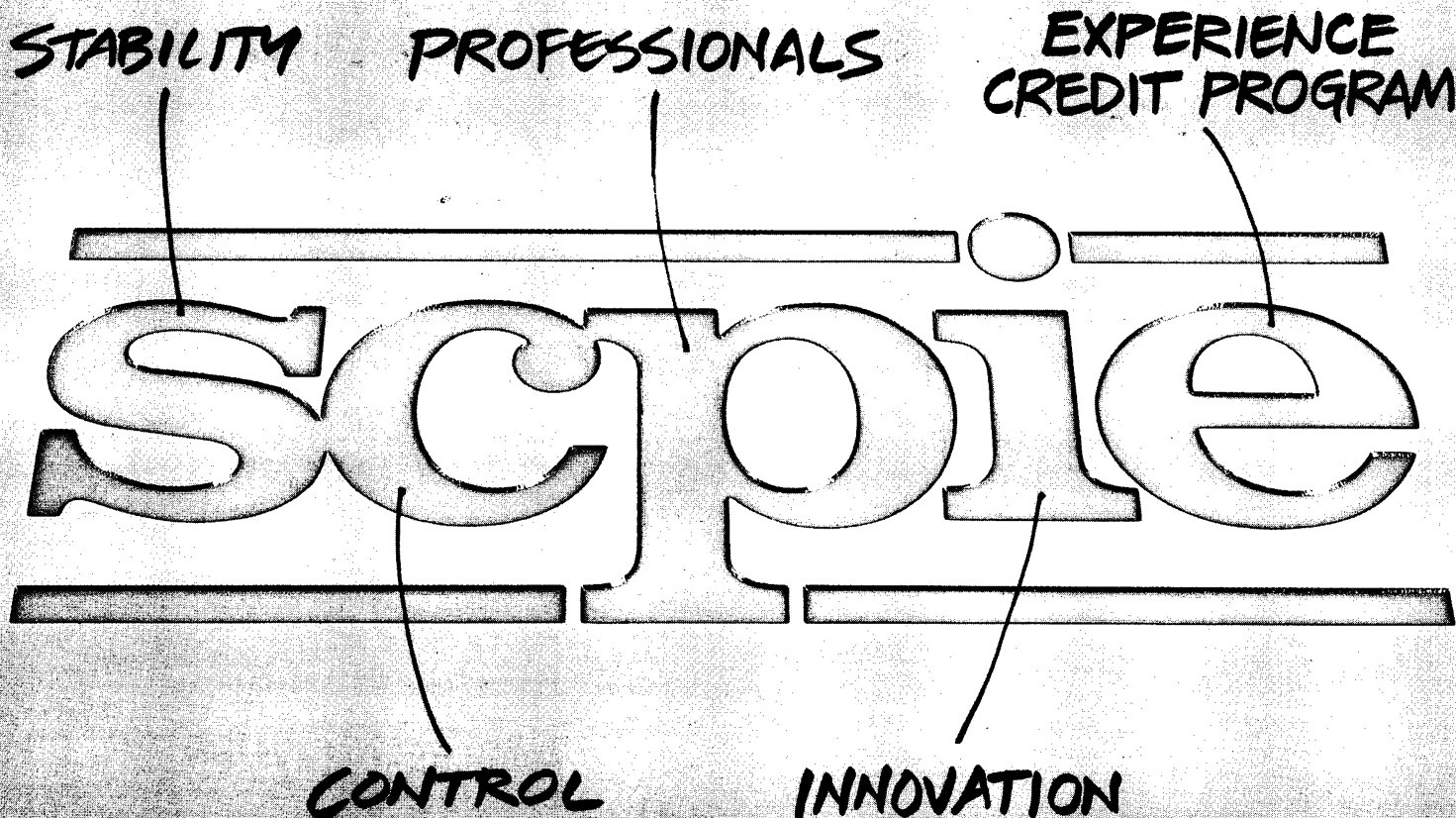
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CARDIZEM® SR (diltiazem hydrochloride) is available as sustained release capsules of 60 mg, 90 mg, and 120 mg in bottles of 100, and in UDIP® packages of 100.

CARDIZEM® CD Product Information as of October 1991

CARDIZEM® SR Product Information as of January 1991

References: 1. Data on file, Marion Merrell Dow Inc. 2. Cramer JA, Mattson RH, Prevey ML, et al. JAMA. 1989;261(32):3273-3274.



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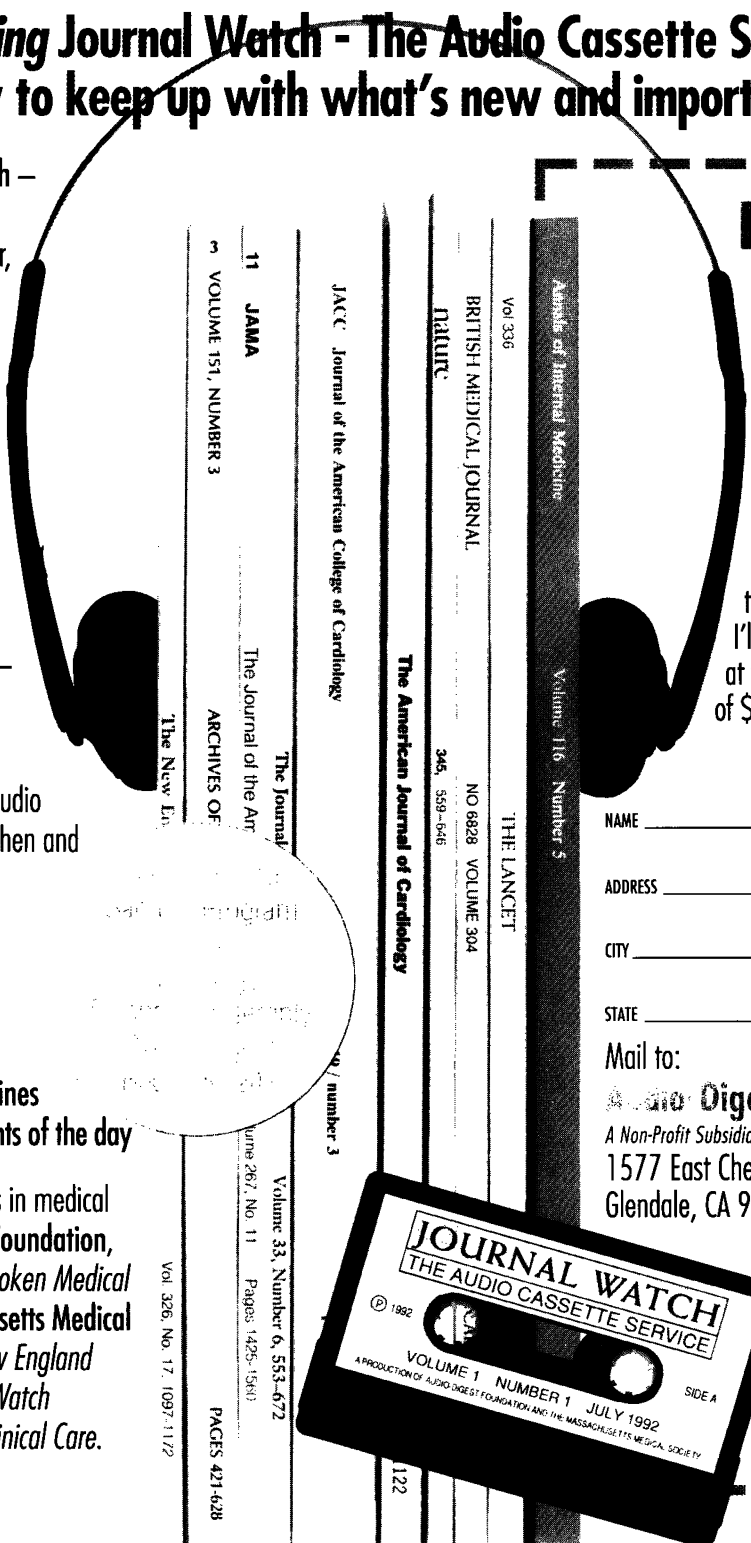
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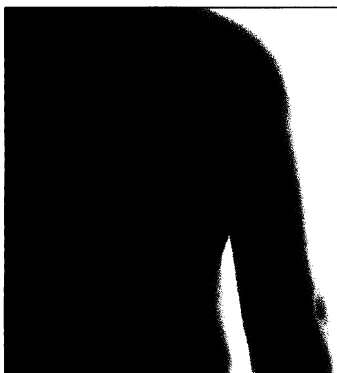
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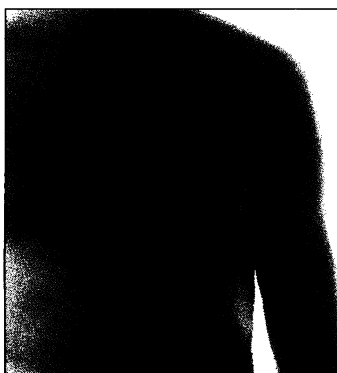
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(isradipine)



Facilitates renal function.

- No clinically significant change in serum creatinine^{1,2} or creatinine clearance^{1,3}
- No clinically significant effect on glomerular filtration rate³⁻⁶
- Maintains or decreases filtration fraction^{1,3,6}



Maintains cardiac performance.

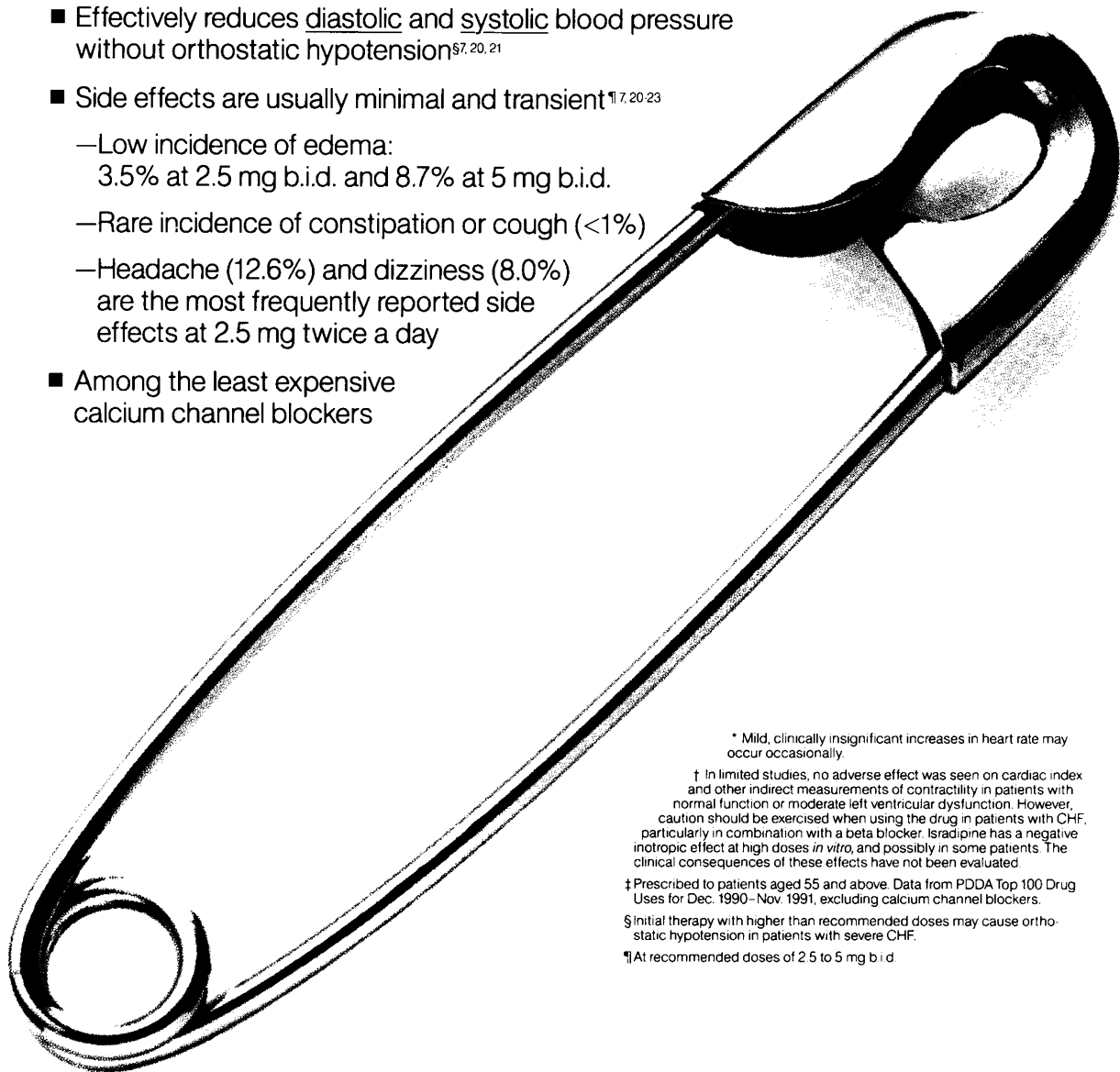
- No significant effect on heart rate^{*7-10}
- No adverse effect on cardiac conduction^{11,12} or contractility^{† 3,10,13-15}
- No alteration of digoxin clearance¹⁶



Does not compromise metabolic parameters.

- No clinically significant effect on serum glucose metabolism¹⁷
- No effect on glucose tolerance, insulin secretion or insulin action in NIDDM patients¹⁷
- No clinically significant effect on lipid metabolism^{18,19}

- No known contraindications except for hypersensitivity to DynaCirc
- No significant interactions with the 20 most-commonly prescribed drugs†
- Effectively reduces diastolic and systolic blood pressure without orthostatic hypotension§7, 20, 21
- Side effects are usually minimal and transient¶7, 20, 23
 - Low incidence of edema:
3.5% at 2.5 mg b.i.d. and 8.7% at 5 mg b.i.d.
 - Rare incidence of constipation or cough (<1%)
 - Headache (12.6%) and dizziness (8.0%) are the most frequently reported side effects at 2.5 mg twice a day
- Among the least expensive calcium channel blockers



* Mild, clinically insignificant increases in heart rate may occur occasionally.

† In limited studies, no adverse effect was seen on cardiac index and other indirect measurements of contractility in patients with normal function or moderate left ventricular dysfunction. However, caution should be exercised when using the drug in patients with CHF, particularly in combination with a beta blocker. Isradipine has a negative inotropic effect at high doses *in vitro*, and possibly in some patients. The clinical consequences of these effects have not been evaluated.

‡ Prescribed to patients aged 55 and above. Data from PDDA Top 100 Drug Uses for Dec. 1990–Nov. 1991, excluding calcium channel blockers.

§ Initial therapy with higher than recommended doses may cause orthostatic hypotension in patients with severe CHF.

¶ At recommended doses of 2.5 to 5 mg b.i.d.

DynaCirc[®]
(isradipine)
2.5 mg capsules 5 mg capsules
For Safety's Sake[™]

BRIEF SUMMARY

Please see package insert for full prescribing information.

DYNACIRC® (isradipine) CAPSULES

INDICATION

DynaCirc® (isradipine) is indicated in the management of hypertension. It may be used alone or concurrently with thiazide-type diuretics.

CONTRAINDICATIONS

DynaCirc® is contraindicated in individuals who have shown hypersensitivity to any of the ingredients in the formulation.

WARNINGS

None

PRECAUTIONS

General: Blood Pressure: Because DynaCirc® decreases peripheral resistance, like other calcium blockers DynaCirc® may occasionally produce symptomatic hypotension. However, symptoms like syncope and severe dizziness have rarely been reported in hypertensive patients administered DynaCirc®, particularly at the initial recommended doses. **Use in Patients with Congestive Heart Failure:** Although acute hemodynamic studies in patients with congestive heart failure have shown that DynaCirc® reduced afterload without impairing myocardial contractility, it has a negative inotropic effect at high doses *in vitro*, and possibly in some patients. Caution should be exercised when using the drug in congestive heart failure patients, particularly in combination with a beta-blocker. **Drug Interactions: Nitroglycerin:** DynaCirc® has been safely coadministered with nitroglycerin. **Hydrochlorothiazide:** A study in normal healthy volunteers has shown that concomitant administration of DynaCirc® and hydrochlorothiazide does not result in altered pharmacokinetics of either drug. In a study in hypertensive patients, addition of isradipine to existing hydrochlorothiazide therapy did not result in any unexpected adverse effects, and isradipine had an additional antihypertensive effect.

Propranolol: In a single dose study in normal volunteers coadministration of propranolol had a small effect on the rate but no effect on the extent of isradipine bioavailability. Coadministration of DynaCirc® resulted in significant increases in AUC (27%) and C_{max} (58%) and decreases in t_{max} (23%) of propranolol. **Digoxin:** The concomitant administration of DynaCirc® and digoxin in a single-dose pharmacokinetic study did not affect renal, non-renal and total body clearance of digoxin. **Fentanyl Anesthesia:** Severe hypotension has been reported during fentanyl anesthesia with concomitant use of a beta blocker and a calcium channel blocker. Even though such interactions have not been seen in clinical studies with DynaCirc®, an increased volume of circulating fluids might be required if such an interaction were to occur. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** Treatment of male rats for 2 years with 2.5, 12.5, or 62.5 mg/kg/day isradipine admixed with the diet resulted in dose dependent increases in the incidence of benign Leydig cell tumors and testicular hyperplasia relative to untreated control animals. A comparable endocrine effect was not evident in male patients receiving therapeutic doses of the drug on a chronic basis. Treatment of mice for two years with 2.5, 15, or 80 mg/kg/day isradipine in the diet showed no evidence of oncogenicity. There was no evidence of mutagenic potential based on the results of a battery of mutagenicity tests. No effect on fertility was observed in male and female rats. **Pregnancy: Pregnancy Category C:** There are no adequate and well controlled studies in pregnant women. DynaCirc® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing Mothers:** It is not known whether DynaCirc® is excreted in human milk. A decision should be made as to whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use:** Safety and effectiveness have not been established in children.

ADVERSE REACTIONS

The adverse reaction rates given below are principally based on controlled hypertension studies, but rarer serious events are derived from all exposures to DynaCirc®, including foreign marketing experience. Most adverse reactions were mild and related to the vasodilatory effects of DynaCirc® (dizziness, edema, palpitations, flushing, tachycardia), and many were transient. About 5% of isradipine patients left studies prematurely because of adverse reactions (vs. 3% of placebo patients and 6% of active control patients), principally due to headache, edema, dizziness, palpitations, and gastrointestinal disturbances. The following adverse reactions have been reported by 1% or greater of patients receiving DynaCirc® at any dose (N=934): headache (13.7%), dizziness (7.3%), edema (7.2%), palpitations (4.0%), fatigue (3.9%), flushing (2.6%), chest pain (2.4%), nausea (1.8%), dyspnea (1.8%), abdominal discomfort (1.7%), tachycardia (1.5%), rash (1.5%), poliakiuria (1.5%), weakness (1.2%), vomiting (1.1%), diarrhea (1.1%). The following adverse events were reported in 0.5-1% of the isradipine-treated patients in hypertension studies, or are rare, but more serious events from this and other data sources, including postmarketing exposure, are shown in italics. The relationship of these adverse events to isradipine administration is uncertain. **Skin:** pruritus, *urticaria*. **Musculoskeletal:** cramps of legs/feet. **Respiratory:** cough. **Cardiovascular:** shortness of breath, hypotension, *atrial fibrillation, ventricular fibrillation, myocardial infarction, heart failure*. **Gastrointestinal:** abdominal discomfort, constipation, diarrhea. **Urogenital:** nocturia. **Nervous System:** drowsiness, insomnia, lethargy, nervousness, impotence, decreased libido, depression, syncope, *paresthesia* (which includes numbness and tingling), *transient ischemic attack, stroke*. **Autonomic:** hyperhidrosis, visual disturbance, dry mouth, numbness. **Miscellaneous:** throat discomfort, *leukopenia, elevated liver function tests*.

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[DECEMBER 31, 1990 DYN-22]

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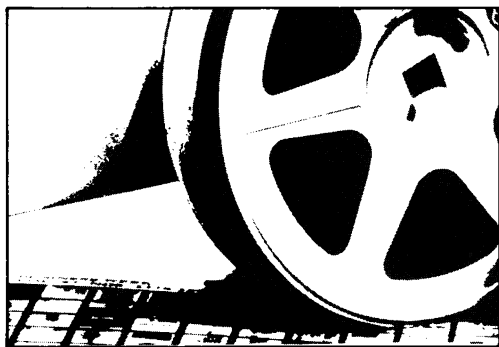
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BuSpar[®] (buspirone HCl)

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Contraindications: Hypersensitivity to buspirone hydrochloride.

Warnings: The administration of BuSpar to a patient taking a monoamine oxidase inhibitor (MAOI) may pose a hazard. Since blood pressure has become elevated when BuSpar was administered concomitantly with an MAOI, such concomitant use is not recommended. BuSpar should not be employed in lieu of appropriate antipsychotic treatment.

Precautions: **General**—Interference with cognitive and motor performance: Although buspirone is less sedating than other anxiolytics and does not produce significant functional impairment, its CNS effects in a given patient may not be predictable; therefore, patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that buspirone does not affect them adversely. Although buspirone has not been shown to increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use with alcohol.

Potential for withdrawal reactions in sedative/hypnotic/anxiolytic drug dependent patients: Because buspirone will not block the withdrawal syndrome often seen with cessation of therapy with benzodiazepines and other common sedative/hypnotic drugs, before starting buspirone withdrawal patients gradually from their prior treatment, especially those who used a CNS depressant chronically. Rebound or withdrawal symptoms may occur over varying time periods, depending in part on the type of drug and its elimination half-life. The withdrawal syndrome can appear as any combination of irritability, anxiety, agitation, insomnia, tremor, abdominal cramps, muscle cramps, vomiting, sweating, flu-like symptoms without fever, and occasionally, even as seizures.

Possible concerns related to buspirone's binding to dopamine receptors: Because buspirone can bind to central dopamine receptors, a question has been raised about its potential to cause acute and chronic changes in dopamine mediated neurological function (eg, dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia). Clinical experience in controlled trials has failed to identify any significant neuroleptic-like activity; however, a syndrome of restlessness, appearing shortly after initiation of treatment, has been reported; the syndrome may be due to increased central noradrenergic activity or may be attributable to dopaminergic effects (ie, represent akathisia).

Information for Patients—Patients should be instructed to inform their physician about any medications, prescription or nonprescription, alcohol or drugs they are now taking or plan to take during treatment with buspirone; to inform their physician if they are pregnant, are planning to become pregnant, or become pregnant while taking buspirone; to inform their physician if they are breast feeding; and not to drive a car or operate potentially dangerous machinery until they experience how this medication affects them.

Drug Interactions—Concomitant use with other CNS active drugs should be approached with caution (see Warnings). Concomitant use with trazodone may have caused 3- to 6-fold elevations of SGPT (ALT) in a few patients. Concomitant administration of BuSpar and haloperidol resulted in increased serum haloperidol concentrations in normal volunteers. The clinical significance is not clear. Buspirone does not displace tightly bound drugs like phenytoin, propranolol, and warfarin from serum proteins, but may displace less firmly bound drugs like digoxin. However, there was one report of prolonged prothrombin time when buspirone was given to a patient also treated with warfarin, phenytoin, phenobarbital, digoxin, and Synthroid.

Carcinogenesis, Mutagenesis, Impairment of Fertility—No evidence of carcinogenic potential was observed in rats or mice; buspirone did not induce point mutations, nor was DNA damage observed; chromosomal aberrations or abnormalities did not occur.

Pregnancy: Teratogenic Effects—Pregnancy Category B: Should be used during pregnancy only if clearly needed.

Nursing Mothers—Administration to nursing women should be avoided if clinically possible.

Pediatric Use—The safety and effectiveness have not been determined in individuals below 18 years of age.

Use in the Elderly—No unusual, adverse, age-related phenomena have been identified in elderly patients receiving a total, modal daily dose of 15 mg.

Use in Patients with Impaired Hepatic or Renal Function—Since buspirone is metabolized by the liver and excreted by the kidneys, it is not recommended in severe hepatic or renal impairment.

Adverse Reactions (See also Precautions): Commonly Observed—The more commonly observed untoward events, not seen at an equivalent incidence in placebo-treated patients, include dizziness, nausea, headache, nervousness, lightheadedness, and excitement.

Associated with Discontinuation of Treatment—The more common events causing discontinuation included: central nervous system disturbances (3.4%), primarily dizziness, insomnia, nervousness, drowsiness, lightheaded feeling; gastrointestinal disturbances (1.2%), primarily nausea; miscellaneous disturbances (1.1%), primarily headache and fatigue. In addition, 3.4% of patients had multiple complaints, none of which could be characterized as primary.

Incidence in Controlled Clinical Trials—Adverse events reported by 1% or more of 477 patients who received buspirone in four-week, controlled trials: **Cardiovascular:** Tachycardia/palpitations 1%. **CNS:** Dizziness 12%, drowsiness 10%, nervousness 5%, insomnia 3%, lightheadedness 3%, decreased concentration 2%, excitement 2%, anger/hostility 2%, confusion 2%, depression 2%. **EENT:** Blurred vision 2%. **Gastrointestinal:** Nausea 8%, dry mouth 3%, abdominal/gastric distress 2%, diarrhea 2%, constipation 1%, vomiting 1%. **Musculoskeletal:** Musculoskeletal aches/pains 1%. **Neurological:** Numbness 2%, paresthesia 1%, incoordination 1%, tremor 1%. **Skin:** Skin rash 1%. **Miscellaneous:** Headache 6%, fatigue 4%, weakness 2%, sweating/clamminess 1%.

Other Events Observed During the Entire Premarketing Evaluation—The relative frequency of all other undesirable events reasonably associated with the use of buspirone in approximately 3000 subjects who took multiple doses of the drug under well-controlled, open, and uncontrolled conditions is defined as follows: Frequent are those occurring in at least 1/100 patients; infrequent are those occurring in 1/100 to 1/1000 patients; and rare are those occurring in less than 1/1000 patients. **Cardiovascular**—frequent: non-specific chest pain; infrequent: syncope, hypotension, hypertension; rare: cerebrovascular accident, congestive heart failure, myocardial infarction, cardiomyopathy, bradycardia. **Central Nervous System**—frequent: dream disturbances; infrequent: depersonalization, dysphoria, noise intolerance, euphoria, akathisia, fearfulness, loss of interest, dissociative reaction, hallucinations, suicidal ideation, seizures; rare: feelings of claustrophobia, cold intolerance, stupor, slurred speech, psychosis. **EENT**—frequent: tinnitus, sore throat, nasal congestion; infrequent: redness and itching of the eyes, altered taste, altered smell, conjunctivitis; rare: inner ear abnormality, eye pain, photophobia, pressure on eyes. **Endocrine**—rare: galactorrhea, thyroid abnormality. **Gastrointestinal**—infrequent: flatulence, anorexia, increased appetite, salivation, irritable colon, rectal bleeding; rare: burning of the tongue. **Genitourinary**—infrequent: urinary frequency, urinary hesitancy, menstrual irregularity and spotting, dysuria; rare: amenorrhea, pelvic inflammatory disease, enuresis, nocturia. **Musculoskeletal**—infrequent: muscle cramps, muscle spasms, rigid/stiff muscles, arthralgias. **Neurological**—infrequent: involuntary movements, slowed reaction time; rare: muscle weakness. **Respiratory**—infrequent: hyperventilation, shortness of breath, chest congestion; rare: epistaxis. **Sexual Function**—infrequent: decreased or increased libido; rare: delayed ejaculation, impotence. **Skin**—infrequent: edema, pruritus, flushing, easy bruising, hair loss, dry skin, facial edema, blisters; rare: acne, thinning of nails. **Clinical Laboratory**—infrequent: increases in hepatic aminotransferases (SGOT, SGPT); rare: eosinophilia, leukopenia, thrombocytopenia. **Miscellaneous**—infrequent: weight gain, fever, roaring sensation in the head, weight loss, malaise; rare: alcohol abuse, bleeding disturbance, loss of voice, hiccoughs.

Postintroduction Clinical Experience—Rare occurrences of allergic reactions, cogwheel rigidity, dystonic reactions, ecchymosis, emotional lability, tunnel vision, and urinary retention have been reported. Because of the uncontrolled nature of these spontaneous reports, a causal relationship to BuSpar has not been determined.

Drug Abuse and Dependence: Controlled Substance Class—Not a controlled substance.

Physical and Psychological Dependence—Buspirone has shown no potential for abuse or diversion and there is no evidence that it causes tolerance, or either physical or psychological dependence. However, since it is difficult to predict from experiments the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of buspirone misuse or abuse (eg, development of tolerance, incrementation of dose, drug-seeking behavior).

Overdosage: Signs and Symptoms—At doses approaching 375 mg/day the following symptoms were observed: nausea, vomiting, dizziness, drowsiness, miosis, and gastric distress. No deaths have been reported in humans either with deliberate or accidental overdosage.

Recommended Overdosage Treatment—General symptomatic and supportive measures should be used along with immediate gastric lavage. No specific antidote is known and dialyzability of buspirone has not been determined.

For complete details, see Prescribing Information or consult your Mead Johnson Pharmaceuticals Representative.

U.S. Patent Nos. 3,717,634 and 4,182,763

MJL8-4270R2

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(buspirone HCl)

**Now indicated
for the relief of
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with coexisting
depressive
symptoms.***

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in anxious patients with or without
coexisting depressive symptoms.²

Relief of anxiety symptoms
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steadily through the fourth week of
therapy.³

Nonaddictive, no more sedation
(10%) than seen with placebo (9%).^{4,5}

The more commonly observed
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(12%), nausea (8%), headache (6%),
and nervousness (5%).

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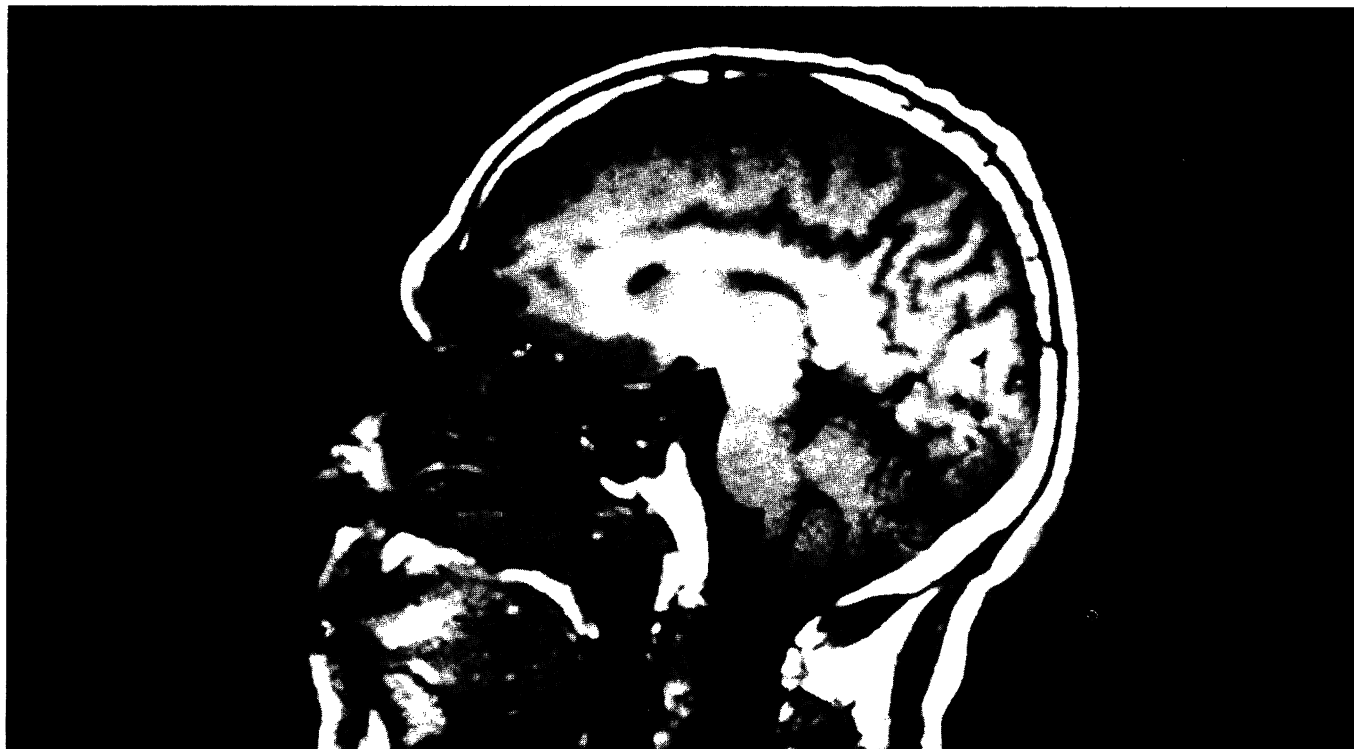


*BuSpar is not indicated for the relief of primary depressive disorder.

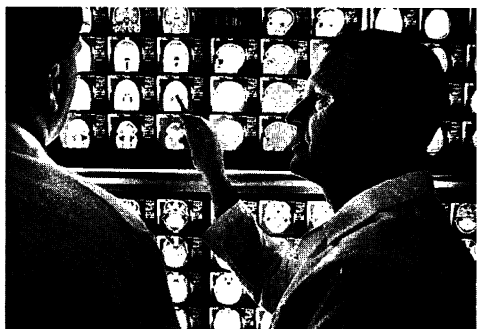
Please see references and brief summary on adjacent page.

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YOU DON'T HAVE TO BE A BRAIN SURGEON TO APPRECIATE OUR NEUROSCIENCE CENTER, BUT IT HELPS.



When we asked Dr. Cully Cobb why he routinely performs neurosurgery at Sutter General Hospital, he explained, "Neurosurgery has become very complex. Multiple specialities overlap and are interdependent. To provide optimal care,



a physician needs a full range of services. Sutter General is one of the few hospitals that offer that kind of support." In fact, Sutter Neuroscience Center at Sutter General Hospital is the only private facility in the region that offers such a wide array in the way of neurology services. Interventional neuroradiology, angiography and neuropathology are available, along with comprehensive epilepsy services and

advanced neurodiagnostics, including intraoperative studies. The six-bed Neuro Observation Unit lets physicians monitor patients' neurologic status, including EEG and intracranial pressure, around the clock. The nursing staff is specially trained in neuroscience. And neuro rehabilitation specialists provide ongoing care

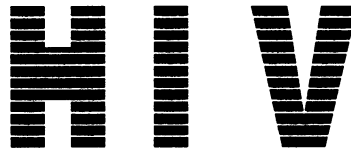


Cully Cobb, M.D.

for patients. As Dr. Cobb puts it, "Many centers emphasize only one area. At Sutter General, there's excellence in every aspect of neurosurgical care. The equipment is top-notch. The facilities are excellent. There are superb physicians. And the operating room and neuroscience staff is outstanding." Then he adds, "Neurosurgery is like a gigantic jigsaw puzzle. If one part is missing, it's a disaster. At Sutter General, all the parts are there. And they work together beautifully." For more information about available services, call Sutter Neuroscience Center at Sutter General Hospital in Sacramento, (916) 733-3049.



Sutter Neuroscience Center
SUTTER GENERAL HOSPITAL



5th NATIONAL AIDS UPDATE CONFERENCE

"Integrating HIV / AIDS: A Shared Responsibility"

October 6 - 9 , 1992 - San Francisco Civic Auditorium and Brooks Hall

Conference Sponsors (partial list)

American Medical Association
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California Medical Association
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National Association of Social Workers
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American Nurses Association
California Association of Public Hospitals
California Nurses Association
National Association of Public Hospitals
National Hospice Organization
United States Conference of Mayors
U.S. Public Health Service/HRSA

The Conference goal is to provide opportunities for dialogue and discussion among those responsible for meeting the special challenges of the HIV epidemic, including:

- health care providers
- hospital administrators
- social workers
- dentists
- community-based and HIV / AIDS service organizations
- public health agencies
- people with HIV / AIDS
- policy-makers
- physicians
- government and community leaders
- mental health practitioners
- pharmacists
- nurses

Plenary and workshop sessions reflecting the various levels of attendee knowledge and expertise bring attention to HIV issues in four Conference tracks:

- Policy and Administration
- Education and Prevention
- Care and Services
- Treatment

Special events include: round table discussions, visual and performing arts, films, posters, exhibits, community site visits and social networking.

To meet its objectives, the Conference will:

- Offer an extensive series of workshops
- Focus on the role of health care providers and common issues affecting all health disciplines providing care for HIV-infected persons
- Discuss effective models of education
- Explore current ethical, legal, administrative and policy issues
- Examine issues related to access and financing
- Present research on recent advances and issues in clinical management
- Emphasize emerging issues related to gay men, ethnic minorities, women and children, adolescents, the elderly, differently-abled, homeless, and IV drug users.

Continuing education credit is available for physicians, nurses and social workers.

For general assistance, to register or exhibit, contact:

KREBS Convention Management Services
555 DeHaro Street, Suite 200, San Francisco, CA 94107-2348
Phone: 415/255-1297 or Fax: 415/255-8496.



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PHYSICIANS WANTED

FAMILY PHYSICIAN—LEWISTON, IDAHO

Opportunity to join Family Practice group. Ambulatory and acute/inpatient care. No OB. Competitive income guarantee with opportunity to join full partnership. Send CV to Clearwater Medical Clinic, 1522 17th St, Lewiston, ID 83501, attn: Peggy Johnson; or call (208) 743-8416.

CALIFORNIA MULTISPECIALTY. Dermatologist, Radiologist, Otorhinolaryngologist, General Surgeon, Cardiologist, Internal Medicine, Pediatrician, Gastroenterologist, Orthopedist, General/Family Practitioner, Obstetrician/Gynecologist. Excellent opportunity for physicians in Los Angeles suburb to join 100 member multispecialty medical group. Large fee-for-service and prepaid practice, no Medi-Cal. Excellent compensation program based on guarantee plus incentive, profit sharing and pension plan. Group provides health, dental, life, and malpractice. Partnership in real estate and medical corporation available. Send CV to Ron McDaniel, Assistant Administrator, Mullikin Medical Center—5, 17821 S. Pioneer Blvd, Artesia, CA 90701.

NEPHROLOGIST WANTS PARTNER/ASSOCIATE BC/BE Gastroenterologist/Cardiologist/Nephrologist/Pulmonologist. Excellent practice, equal partnership opportunity without buy-in or overhead. Send CV to Dr M. Streger, 27800 Medical Center Rd, Ste 122, Mission Viejo, CA 92691.

POSITIONS AVAILABLE FOR EMERGENCY PHYSICIANS WORKING PM SHIFTS. Hourly differential paid in addition to fee-for-service compensation. Shifts vary from seven to nine hours in length. Excellent fringe benefits. Malpractice paid. Contact Nancy C. Kendall at SPEMG, Inc, 8350 Auburn Blvd, Ste 100, Citrus Heights, CA 95610; or call (916) 727-1049 for more information.

BC/BE GASTROENTEROLOGIST NEEDED. Busy office practice. 27 doctor multispecialty clinic. Mountain locale. Guaranteed salary. Excellent benefits. CV to Mike McCraley, Ogden Clinic, 4650 Harrison, Ogden, UT 84403; (800) 234-5637.

BC/BE GENERAL INTERNIST NEEDED. Nine physician department in 27 doctor multispecialty clinic. Guaranteed salary. Excellent benefits. CV to Mike McCraley, Ogden Clinic, 4650 Harrison, Ogden, UT 84403; (800) 234-5637.

PHYSICIANS WANTED

Western States OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 300 positions of various specialties. Both permanent and locum tenens. Send CV to Western States Physician Services, 5627 E. Kings Canyon, Ste 156, Fresno, CA 93727, or call 1 (800) 873-0786.

PRIMARY CARE PHYSICIAN wanted for expanding eastern Washington clinic. Full- and part-time positions available. Located in prime recreational area. Skiing, sailing, fishing, hunting all within a short distance. Enjoy mild climate, excellent schools and a major university branch campus in growing community of 100,000 plus. Challenging work in a superbly equipped clinic with state-of-the-art lab, x-ray, laser, and endoscopy. Above average compensation and benefits including malpractice, health insurance, and CME. Contact Dr Stephen L. Smith, 310 Torbett, Richland, WA 99352; (509) 545-8340 or FAX (509) 946-7666.

SOUTHERN CALIFORNIA. Family Practice physician position available in Riverside County. Guaranteed income, excellent benefits with early partnership. Send résumé to Number 265, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PEDIATRICIAN—SANTA MONICA. Associate needed for rapid takeover of busy, lucrative Pediatric practice. Good coverage weekends. Low overhead. Rare opportunity. Phone Lisa; (310) 829-1752 for details.

NORTHERN CALIFORNIA

San Jose's leading multispecialty group is growing. We are seeking BE/BC physicians in the following specialties:

- Orthopedic Surgery
- Internal Medicine/General
- Pediatrics
- Urgent Care
- Family Practice
- Occupational Medicine
- Radiology
- Internal Medicine/Gastroenterology
- General Surgery

If you are committed to excellence and strongly motivated for success, we would like to hear from you. Please send your CV to Maureen Forrester, San Jose Medical Group, Inc*, 45 S. 17th St, San Jose, CA 95112; or call (408) 282-7833.

*An independent physician group affiliated with Stanford University Medical Center.

PHYSICIANS WANTED



PHYSICIANS NEEDED

The continuing growth of our service area population (now 105,000) has created an immediate need for additional BC/BE physicians in the following specialties:

- FAMILY PRACTICE
- ORTHOPEDIC SURGERY
- OTOLARYNGOLOGY
- PEDIATRICS

These excellent practice opportunities offer guaranteed income and a strong referral base.

112-bed full service hospital, very well equipped. Excellent ancillary services. Our service area population is now 105,000; a growing area with new businesses and a stable economy. A 30% plus growth in population and jobs is predicted for our area during 1990s.

Located in central California near Sequoia National park, Tulare offers an excellent family oriented lifestyle and all expected amenities. Beautiful homes, close to hospital and office, are affordably priced. Good schools, many community activities, and abundant recreation including golf, tennis, skiing, mountain and equestrian activities. Easy access to all California's major metropolitan and resort areas.

Contact:

Tulare District Hospital
Physician Recruiting Office
PO Box 90112
Los Angeles, CA 90009
(800) 468-2687



AMBULATORY CARE, Hayward, Modesto, Orange County, California. Thriving practices, attractive facilities, competitive salary, profit-sharing, partnership with growth potential. Contact John Gravette, California Emergency Physicians, 2101 Webster St, #1050, Oakland, CA 94612; (510) 835-7431. Outside of California, (800) 842-2619.

SALT LAKE CITY—URGENT CARE/FAMILY PRACTICE. Six year old center in upper middle class community. BC preferred, early partnership available. Great recreation area. Work Net, PO Box 26692, Salt Lake City, UT 84199.

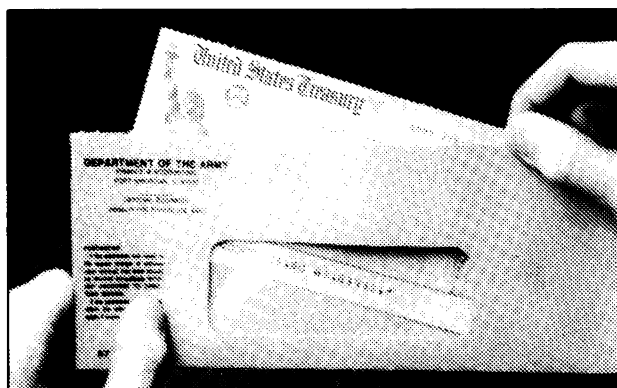
FULL-TIME EMERGENCY PHYSICIANS to join a Level 11 trauma center. Active practice, 39,000 visits annually. Double coverage 24 hours with additional physician coverage during peak hours. Opportunities available for administrative, teaching, and pre-hospital direction. Located in urban community with significant cultural, recreational, and education resources available. Send CV to Director, PO Box 80412, Phoenix, AZ 85060-0412.

TIME TO CHANGE YOUR LIFESTYLE. Thomas-Davis Medical Centers, an expanding multispecialty group of 180 plus physicians, needs Pediatrics, Internal Medicine, Family Practice, OB/GYN, Urgent Care, General Surgery, Orthopedic Surgery, Urology, Otolaryngology, Ophthalmology, and Retina specialists. Top benefits, profit sharing, guarantee first two years, plus incentive pay, early shareholder. Fee-for-service plus HMO. BE/BC. Call or write Bill De Long; (800) 658-9166, TDMC, PO Box 12650, Tucson, AZ 85732.

CALIFORNIA, PACIFIC NORTHWEST, ARIZONA. Positions in Family Practice, Internal Medicine, Orthopedics, Pediatrics and OB/GYN. Call or send confidential CV to Mitchell & Associates, Inc, PO Box 1804, Scottsdale, AZ 85252; (602) 990-8080.

(Continued on Page 380)

ANESTHESIOLOGISTS AND SURGEONS: COULD YOU USE AN EXTRA \$12,500?



If you're a resident in anesthesiology or surgery, a \$9,500 yearly stipend plus your Reserve pay could total \$12,500 in the Army Reserve's Specialized Training Assistance Program (STRAP).

You will have opportunities to continue your education and attend conferences, and we will be flexible about scheduling the time you serve. Your immediate commitment could be as little as two weeks a year, with a small added obligation later on.

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(Continued from Page 378)

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PRACTICE TOGETHER in this semi-rural community located 15 miles west of Spokane, Washington.

ADVANTAGES:

- Affiliation and support from a 75 physician multispecialty group.
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- Up-to-date, modern clinic with a well-trained staff.
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SOUTHERN CALIFORNIA

Several positions available to join a multispecialty group, partnership as well as solo practice for the explosive growth of our area population. BC/BE physician in such specialties as:

- FAMILY PRACTICE
- PEDIATRICS
- OB/GYN
- INTERNAL MEDICINE

These excellent practice opportunities offer guaranteed income and a strong referral base.

Strategic location in the Inland Empire minutes from Palm Springs, mountain resorts, Newport Beach, and Los Angeles. University affiliation available.

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St. Bernardine Medical Center
Janis Pryor, Director Business Development/Provider Relations
or Julie Wagner, Provider Relations Coordinator
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San Bernardino, CA 92404
(714) 883-8711, ext 3063

PUBLIC NOTICE

Department of Corrections
WASCO STATE PRISON
RECEPTION CENTER

701 Scofield Ave, Wasco, CA 93280

The Wasco State Prison Reception Center is accepting applications from Medical Doctors in the fields of General Practice and Internal Medicine to perform medical services to the inmate population on a part-time contractual basis.

Applicants must be fully licensed medical practitioners in the State of California.

Hours of work and compensation will be negotiated at the time of interview. To set up an interview with the Chief Medical Officer, Dr George Girgis, please contact:

Christine McAvoy
(805) 758-8400, ext 5908

Wasco State Prison is located approximately three miles west of the City of Wasco on State Highway 46. The institution houses 4,000 to 4,500 inmates of varying custody levels.

Duties will consist of but not be limited to:

- Diagnostic and general medicine
- Physicals on newly committed inmates
- Emergency medicine
- Daily clinics and sick call

(Continued on Page 381)

Physician Leaders Los Angeles and Orange Counties

CIGNA Healthplans of CA is accepting curricula vitae for the position of Chief of Staff for several Health Care Centers which are part of CIGNA's 350,000 member Health Maintenance Organization.

The Chief of Staff is the senior manager and leader of the Center and has clinical as well as management responsibilities. Board Certification and CA licensure are required.

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Contact: **Director, Professional Recruitment**
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A little time off sounded really good. And he thinks being exposed to different types of medical practice will serve him well when he returns to his hometown to establish a community health center.

A singer. A board-certified family practitioner. Soft-spoken for a New Yorker. Ron Richmond knows...

It's a great way to
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Salt Lake City ■ Atlanta ■ Grand Rapids, Mich.

(Continued from Page 380)

PHYSICIANS WANTED

PHYSICIAN OPPORTUNITIES NATIONWIDE

For all specialties for hospitals, clinics, multi-specialty groups, partnership and solos. Contact Jim Grant in complete confidence at the bay area specialists. **G & G Physician Services, 1400 Coleman, Ste B-22, Santa Clara, CA 95050; or call (800) 727-2478, FAX (408) 727-7390.** Never a fee to the physician.

ROCKY MOUNTAIN WEST AND SOUTHWEST NEED PHYSICIANS. All specialties needed. Urban, rural, solo, group opportunities, all close to mountain recreation. Call Rita Longino at (800) 279-5267 or FAX CV to (800) 467-1246 or send CV to WHS, PO Box 2107, Corrales, NM 87048-2107.

NORTHERN CALIFORNIA RECREATION AREA. Full-time and part-time salaried position in Ambulatory Care clinic. Enjoy excellent working hours, no night calls, generous benefit package, malpractice insurance provided. Located near the Sierra foothills offering excellent opportunities for hiking, swimming, boating, fishing, and skiing. California license required. Family Practitioner preferred. Call or send résumé to Northern Valley Indian Health, Inc, 2167 Montgomery St, Oroville, CA 95965; (916) 534-8440. EOE Native Americans encouraged to apply. Deadline: open until filled.

INTERNAL MEDICINE BC/BE OPENING due to retirement. Very stable multispecialty group in growing area. Will join department of eight other Internal Medicine physicians. New building on hospital campus. McHenry Medical Group Inc, Attention Thomas Wallace, MD, PO Box 576566, Modesto, CA 95357.

MONTEREY, CALIFORNIA. BC/BE Internist needed to replace retiring partner in busy four member group. Reply to Number 273, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PHYSICIANS WANTED

NORTHERN CALIFORNIA

SAN JOSE. Leading Primary Care group practice affiliated with 200-bed hospital is growing. BE/BC physicians in the following specialties are needed:

- Family Practice
- Internal Medicine
- Pediatrics
- OB/GYN

A generous salary, good benefits, and a liveable practice schedule are offered. Please send your CV to **Ken Baker, Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111; or call (800) 229-0411 or (415) 399-8840; FAX (415) 399-0411.**

INTERNAL MEDICINE—NEVADA, TEXAS, LOUISIANA, FLORIDA! Private practice opportunities available in Las Vegas and Reno, Nevada; Dallas, Victoria, and McAllen, Texas; New Orleans and Shreveport, Louisiana; West Palm Beach, Hollywood, and Plantation, Florida. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft Worth, TX 76185, or FAX (817) 927-0030.

PEDIATRICIANS—NEVADA, CALIFORNIA, TEXAS! Private practice opportunities available. Hospital sponsored with coverage or join an established group. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft Worth, TX 76185, or FAX (817) 927-0030.

FAMILY PRACTICE—CALIFORNIA, NEVADA, LOUISIANA, AND TEXAS! Private practice opportunities available in southern California, Las Vegas and Reno, Nevada, Shreveport and New Orleans, Louisiana with established groups. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft Worth, TX 76185, or FAX (817) 927-0030.

PHYSICIANS WANTED

OB/GYN. Multispecialty group in northwest Washington desires second Obstetrician. Excellent practice opportunity, full range of benefits, early partnership status, all practice costs paid. For more information contact Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

WASHINGTON. Openings for career oriented Emergency Physicians, BC in Emergency or Primary medical specialty. Seattle metropolitan hospital with 54,000 annual visits. Excellent salary in a stable growing group. Contact Dan Hiatt in care of Linda Johnson, 8009 S. 180th, Ste 110, Kent, WA 98032; (206) 575-2595.

OTOLARYNGOLOGIST. BC/BE to join 28 physician multispecialty group practice. Located in beautiful Pacific northwest between Seattle and Vancouver, BC. Contact Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273.

FAMILY PRACTICE PHYSICIAN. Full-time in a busy walk-in medical clinic. Located in Visalia, California (Tulare County). Malpractice insurance, good salary, etc. Please call (209) 627-5555 for more information.

ASSOCIATE IN PEDIATRICS. Kern Medical Center, Bakersfield, California, a teaching hospital affiliated with UCLA and UCI Schools of Medicine, seeks an Associate in the Division of Pediatrics. Prerequisites include eligibility or certification by the American Board of Pediatrics, strong interest in teaching and qualifications for faculty appointment in UCLA Department of Pediatrics. Comprehensive salary and benefit package. A part-time private practice is permitted. Medical center is in central California, a mid-sized urban community with moderate cost of living. Send CV and inquiries to Navin Amin, MD, Chairman, Department of Family Practice/Pediatrics, Kern Medical Center, 1830 Flower St, Bakersfield, CA 93305.

(Continued on Page 382)

(Continued from Page 381)

PHYSICIANS WANTED

JUST SAY "NO"

... to long commutes, traffic jams, high crime and "YES" to an exceptional practice opportunity for you and great quality of life for your family. Dakota Clinic in Fargo, North Dakota, has exceptional practice opportunities in its North Dakota and Western Minnesota locations in the following specialties:

- CARDIOTHORACIC SURGERY
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- GENERAL SURGERY
- INTERNAL MEDICINE
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- OB/GYN
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- ORTHOPEDICS
- OTOLARYNGOLOGY
- PEDIATRICS
- PSYCHIATRY
- RADIATION ONCOLOGY
- RADIOLOGY

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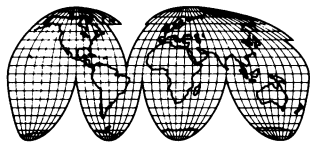
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(Continued on Page 383)

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(Continued from Page 383)

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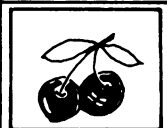
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GILROY, CALIFORNIA. BC INTERNIST to join established but growing private practice in Gilroy, California. Ideal candidate will have one to two years practice experience. Guaranteed salary and benefits. Excellent practice opportunity in this growing community. Send CV to Number 272, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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BC/BE OB/GYN AND FAMILY PRACTITIONER with commitment to caring for the underserved, needed to join one Family Nurse Practitioner, one Pediatric Nurse Practitioner, and one OB/GYN Nurse Practitioner in Walla Walla, Washington. Shared call with two local OB/GYNs and four Family Physicians. Diverse cultural influences. Rural setting, abundant recreational opportunities. Competitive salary, NHSC loan repayment slots, professional liability, excellent benefit package including vacation up to 32 days per year. Contact Ann Garza, Director of Personnel, or Jeri Weeks, Personnel Assistant, (509) 865-5898, or Sylvia Arroyo, Clinic Administrator, (509) 525-6650.

INTERNIST BC/BE to join 10 physician (OB, Pediatrics, Internal Medicine), Primary Care community health clinic in Toppenish, Washington serving migrant and seasonal farm workers with common as well as Third World maladies. Reasonable call schedule with 3.5 Internal Medicine department. Rural setting, beautiful, sunny central Washington near Columbia River Gorge. Diverse cultural influences (Hispanic and Native American). Recreational opportunities including fishing, skiing, and bikers' paradise. Competitive salary with excellent benefit package including vacation up to 32 days per year and professional liability. Contact Ann Garza, Director of Personnel, Yakima Valley Farm Workers Clinic, PO Box 190, Toppenish, WA 98948; (509) 865-5898.

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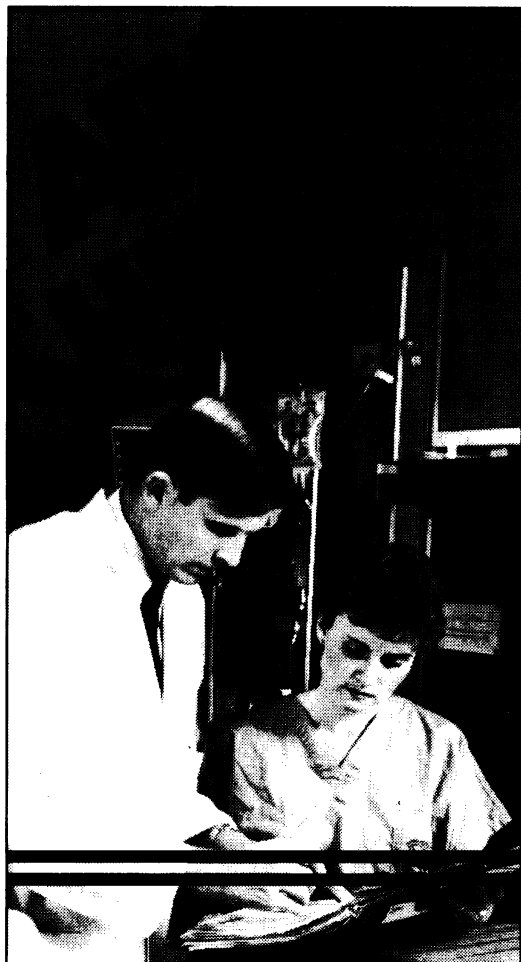
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NORTHERN CALIFORNIA HOSPITAL seeking a BC/BE Internist to staff its new satellite medical clinics. Assistance is available in establishing a practice. Net income guarantees are open including support for office staff and required equipment. Contact Margaret Ward, Redbud Community Hospital, PO Box 6720, Clearlake, CA 95422; (707) 994-6486, ext 128.

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(Continued on Page 388)

(Continued from Page 387)

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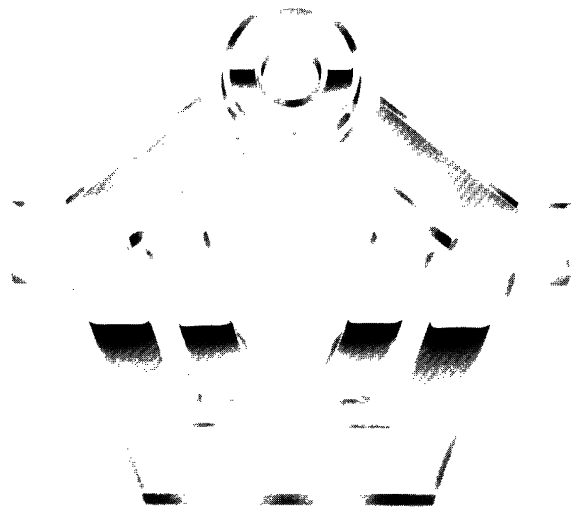
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One Of A Kind

Zantac®

ranitidine HCl/Glaxo 150 mg and 300 mg tablets

Zantac® 150 Tablets
(ranitidine hydrochloride)

Zantac® 300 Tablets
(ranitidine hydrochloride)

Zantac® Syrup
(ranitidine hydrochloride)

The following is a brief summary only. Before prescribing, see complete prescribing information in Zantac® product labeling.

INDICATIONS AND USAGE: Zantac® is indicated in:

1. Short-term treatment of **active duodenal ulcer**. Most patients heal within 4 weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (e.g., Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within 6 weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD)**. Symptomatic relief commonly occurs within 1 or 2 weeks after starting therapy with Zantac 150 mg b.i.d.
6. Treatment of endoscopically diagnosed **erosive esophagitis**. Healing of endoscopically diagnosed erosive esophagitis occurs at 4 weeks (47%), 8 weeks (71%), and 12 weeks (84%) of therapy with Zantac 150 mg q.i.d. Symptomatic relief of heartburn commonly occurs within 24 hours of therapy initiation with Zantac.

Concomitant antacids should be given as needed for pain relief to patients with active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; GERD; and erosive esophagitis.

CONTRAINDICATIONS: Zantac® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to Zantac® therapy does not preclude the presence of gastric malignancy.

2. Since Zantac is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see DOSAGE AND ADMINISTRATION). Caution should be observed in patients with hepatic dysfunction since Zantac is metabolized in the liver.

Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during Zantac therapy, and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although Zantac has been reported to bind weakly to cytochrome P-450 *in vitro*, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions that suggest that Zantac may affect the bioavailability of certain drugs by some mechanism as yet unidentified (e.g., a pH-dependent effect on absorption or a change in volume of distribution).

Increased or decreased prothrombin times have been reported during concurrent use of ranitidine and warfarin. However, in human pharmacokinetic studies with dosages of ranitidine up to 400 mg per day, no interaction occurred; ranitidine had no effect on warfarin clearance or prothrombin time. The possibility of an interaction with warfarin at dosages of ranitidine higher than 400 mg per day has not been investigated.

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in life-span studies in mice and rats at dosages up to 2,000 mg/kg per day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella*, *Escherichia coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of two matings per week for the next 9 weeks.

Pregnancy: Teratogenic Effects: Pregnancy Category B: Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Zantac. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Zantac is secreted in human milk. Caution should be exercised when Zantac is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Use in Elderly Patients: Ulcer healing rates in elderly patients (65-82 years of age) were no different from those in younger age-groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age-groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with Zantac®. The relationship to Zantac therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to Zantac administration.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported. Rare reports of reversible involuntary motor disturbances have been received.

Cardiovascular: As with other H₂-blockers, rare reports of arrhythmias such as tachycardia, bradycardia, atrioventricular block, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea/vomiting, abdominal discomfort/pain, and rare reports of pancreatitis.

Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg q.i.d. intravenously for 7 days, and in 4 of 24 subjects receiving 50

BRIEF SUMMARY

Zantac® 150 and 300 (ranitidine hydrochloride) Tablets
Zantac® (ranitidine hydrochloride) Syrup

mg q.i.d. intravenously for 5 days. There have been occasional reports of hepatitis, hepatocellular or hepatocellular or mixed, with or without jaundice. In such circumstances, ranitidine should be immediately discontinued. These events are usually reversible, but in exceedingly rare circumstances death has occurred.

Musculoskeletal: Rare reports of arthralgias.

Hematologic: Blood count changes (leukopenia, granulocytopenia, and thrombocytopenia) have occurred in a few patients. These were usually reversible. Rare cases of agranulocytosis, pancytopenia, sometimes with marrow hypoplasia, and aplastic anemia and exceedingly rare cases of acquired immune hemolytic anemia have been reported.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by Zantac and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when Zantac has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving Zantac, but the incidence did not differ from that in the general population.

Integumentary: Rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia.

Other: Rare cases of hypersensitivity reactions (e.g., bronchospasm, fever, rash, eosinophilia), anaphylaxis, angioneurotic edema, and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: (See complete prescribing information in Zantac® product labeling.)

Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice daily. An alternative dosage of 300 mg or 20 mL (4 teaspoonfuls equivalent to 300 mg of ranitidine) once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome): The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day. In some patients it may be necessary to administer Zantac® 150-mg doses more frequently. Dosages should be adjusted to individual patient needs, and should continue as long as clinically indicated. Dosages up to 6 g per day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day.

GERD: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day.

Erosive Esophagitis: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) four times a day.

Dosage Adjustment for Patients With Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with Zantac, the recommended dosage in patients with a creatinine clearance less than 50 mL per minute is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosing schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: Zantac® 150 Tablets (ranitidine HCl equivalent to 150 mg of ranitidine) are peach, film-coated, five-sided tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 (NDC 0173-0344-42) and 100 (NDC 0173-0344-09) tablets and unit dose packs of 100 (NDC 0173-0344-47) tablets.

Zantac® 300 Tablets (ranitidine HCl equivalent to 300 mg of ranitidine) are yellow, film-coated, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) tablets and unit dose packs of 100 (NDC 0173-0393-47) tablets.

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

Zantac® Syrup, a clear, peppermint-flavored liquid, contains 16.8 mg of ranitidine HCl equivalent to 15 mg of ranitidine per 1 mL in bottles of 16 fluid ounces (one pint) (NDC 0173-0383-54).

Store between 4° and 25°C (39° and 77°F). Dispense in light-resistant containers as defined in the USP/NF.

May 1992
2130A



Zantac® 150 Tablets/Zantac® 300 Tablets:
Glaxo Pharmaceuticals, Research Triangle Park, NC 27709

Zantac® Syrup:
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Zantac[®]
ranitidine HCl/Glaxo 150 mg and 300 mg tablets

Please see Brief Summary of Prescribing Information on adjacent page.

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